

The Diagnostic Accuracy of Plasma Neutrophil Gelatinase–Associated Lipocalin in the Prediction of Acute Kidney Injury in Emergency Department Patients With Suspected Sepsis

Nathan I. Shapiro, MD, MPH, Stephen Trzeciak, MD, MPH, Judd E. Hollander, MD, Robert Birkhahn, MD, Ronny Otero, MD, Tiffany M. Osborn, MD, Eugene Moretti, MD, MHSc, H. Bryant Nguyen, MD, Kyle Gunnerson, MD, David Milzman, MD, David F. Gaieski, MD, Munish Goyal, MD, Charles B. Cairns, MD, Kenneth Kupfer, PhD, Seok-Won Lee, PhD, Emanuel P. Rivers, MD, MPH

From the Beth Israel Deaconess Medical Center, Boston, MA (Shapiro); the Cooper University Hospital, Camden, NJ (Trzeciak); the University of Pennsylvania, Philadelphia, PA (Hollander, Gaieski, Goyal); the New York Methodist Hospital, Brooklyn, NY (Birkhahn); the Henry Ford Health System, Detroit, MI (Otero, Rivers); the University of Virginia, Charlottesville, VA (Osborn); the Duke University Medical Center, Durham, NC (Moretti, Cairns); the Loma Linda University Medical Center, Loma Linda, CA (Nguyen); the Virginia Commonwealth University, Richmond, VA (Gunnerson); Biosite Incorporated, San Diego, CA (Kupfer, Lee); and Georgetown University Medical School/Washington Hospital Center, Washington, DC (Milzman).

Study objective: We assess the diagnostic accuracy of plasma neutrophil gelatinase–associated lipocalin (NGAL) to predict acute kidney injury in emergency department (ED) patients with suspected sepsis.

Methods: We conducted a secondary analysis of a prospective observational study of a convenience sample of patients from 10 academic medical center EDs. Inclusion criteria were adult patients aged 18 years or older, with suspected infection or a serum lactate level greater than 2.5 mmol/L; 2 or more systemic inflammatory response syndrome criteria; and a subsequent serum creatinine level obtained within 12 to 72 hours of enrollment. Exclusion criteria were pregnancy, do-not-resuscitate status, cardiac arrest, or dialysis dependency. NGAL was measured in plasma collected at ED presentation. Acute kidney injury was defined as an increase in serum creatinine measurement of greater than 0.5 mg/dL during 72 hours.

Results: There were 661 patient enrolled, with 24 cases (3.6%) of acute kidney injury that developed within 72 hours after ED presentation. Median plasma NGAL levels were 134 ng/mL (interquartile range 57 to 277 ng/mL) in patients without acute kidney injury and 456 ng/mL (interquartile range 296 to 727 ng/mL) in patients with acute kidney injury. Plasma NGAL concentrations of greater than 150 ng/mL were 96% sensitive (95% confidence interval [CI] 79% to 100%) and 51% (95% CI 47% to 55%) specific for acute kidney injury. In comparison, to achieve equivalent sensitivity with initial serum creatinine level at ED presentation required a cutoff of 0.7 mg/dL and resulted in specificity of 17% (95% CI 14% to 20%).

Conclusion: In this preliminary investigation, increased plasma NGAL concentrations measured on presentation to the ED in patients with suspected sepsis were associated with the development of acute kidney injury. Our findings support NGAL as a promising new biomarker for acute kidney injury; however, further research is warranted. [Ann Emerg Med. 2010;56:52-59.]

Please see page 53 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Although acute kidney injury is a pivotal element part of morbidity and mortality in disease and critical illness, there have been few advancements in acute kidney injury diagnosis during the last 40 years. Currently, there is no methodology or laboratory test that detects kidney injury when it occurs. Serum

creatinine level, the current criterion standard of diagnosis in acute kidney injury, is a marker that estimates glomerular filtration rate and reflects a decrease in renal function after it has already occurred. The increase of serum creatinine levels in response to kidney injury can be delayed by up to several days, and increases may not occur until renal function is already impaired. When acute kidney injury requiring renal replacement therapy occurs in critically ill patients, the associated mortality rates can be as high as 80%. Current

Editor's Capsule Summary

What is already known on this topic

Acute kidney injury is common in severe infection. At present, there are no biomarkers that accurately detect its presence before increase of the creatinine level.

What question this study addressed

This 661-patient observational study tested the diagnostic performance of neutrophil gelatinase–associated lipocalin (NGAL) to detect acute kidney injury in emergency department patients with suspected infection.

What this study adds to our knowledge

Plasma concentrations of NGAL greater than 150 ng/dL were 96% sensitive and 51% specific for acute kidney injury occurring within the first 72 hours of hospitalization.

How this might change clinical practice

These preliminary results should not change clinical practice but suggest that NGAL may be useful for identifying patients at risk for acute kidney injury.

research indicates that early interventions for acute kidney injury may produce more favorable outcomes. Thus, biomarkers that increase as an early indicator of acute kidney injury provide the promise of achieving early identification and intervention for these patients.

Importance

Plasma neutrophil gelatinase–associated lipocalin (NGAL) is a member of the lipocalin family of proteins. NGAL is produced in the kidney after ischemic or nephrotoxic injury.^{1–3} Several recent studies demonstrate that NGAL levels measured in both the plasma and the urine of patients represent a novel specific biomarker for the early identification of acute kidney injury after cardiac surgery.^{4–8} In those studies, in patients who subsequently met the criteria for acute kidney injury (defined as a 50% or greater increase in serum creatinine level), NGAL concentrations were markedly increased within a few hours of cardiopulmonary bypass surgery. Patients who present to the emergency department (ED) with suspected infections are at particularly high risk for developing acute kidney injury, and in these patients the consequences can be devastating. Acute kidney injury may also herald the onset of critical illness, given the link between acute kidney injury and death; therefore, it could also have the capacity to affect triage decisions. Additionally, earlier detection may lead to earlier intervention or more focused efforts to restrict nephrotoxic agents such as intravenous contrast dye or certain antibiotics that would

propagate injury.⁹ Although it appears that NGAL holds promise for the early detection of acute kidney injury, there is a clear need for further study. ED patients represent a unique study population because their illnesses are often uncharacterized, and kidney injury is often evolving. Thus, the ability to better detect kidney damage in the most proximal phase of a patient's hospitalization may offer morbidity and mortality benefits through early intervention.

Goals of This Investigation

The objective of this study was to assess the diagnostic accuracy of plasma concentrations of NGAL to predict acute kidney injury in ED patients with suspected sepsis.

MATERIALS AND METHODS

Study Design and Setting

This was a secondary analysis of a prospective, multicenter, observational cohort study of a convenience sample of ED patients with suspected sepsis, following previously described methodology.¹⁰ There were 10 academic centers in the United States that participated during an 18-month period. The trial was approved by the Institutional Review Board for Human Research at each participating center.

Selection of Participants

Inclusion criteria were ED patients aged 18 years or older, a presumptive source of infection suspected by the treating clinician or a serum lactate level greater than 2.5 mmol/L, and 2 of 4 criteria for the systemic inflammatory response syndrome. The systemic inflammatory response syndrome was defined as (1) a temperature greater than 38°C (100.4°F) or less than 36°C (96.8°F); (2) respirations greater than 20 breaths/min or partial pressure of carbon dioxide of less than 32 mm Hg; (3) a pulse rate greater than 90 beats/min; and (4) a WBC count greater than 12,000 cells/mm³ or less than 4,000 cells/mm³ or greater than 10% immature forms.¹¹ Study exclusion criteria were pregnancy, do-not-resuscitate status, or cardiac arrest. For the analysis of acute renal dysfunction, the population was further restricted to exclude all patients with a history of chronic dialysis and to include only patients who had at least 1 follow-up serum creatinine measurement as part of routine clinical care within 12 to 72 hours of presentation (to ascertain the outcome of acute kidney injury).

Data Collection and Processing

We prospectively collected pertinent data on enrollment, including demographics (age, sex, race), comorbid conditions (eg, hypertension, cirrhosis, end-stage renal disease, chronic dialysis, cardiovascular disease, stroke, presence of an immunocompromising illness), social factors (history of smoking or alcohol use), vital signs (pulse rate, blood pressure, respiratory rate, oxygen saturation, temperature), the results of laboratory testing (WBC count, serum blood urea nitrogen level, serum creatinine level, serum lactate level, electrolytes used

to calculate an anion gap [sodium + potassium – chloride]), and the suspected source of infection. During the subsequent 72-hour period from enrollment, we collected serial biophysical data, including vital signs and the results of available laboratory testing. On hospital discharge, we collected discharge vital status (dead or alive).

Methods of Measurement

After written informed consent was obtained, venous whole blood was collected in tubes containing ethylenediaminetetraacetic acid as an anticoagulant. In less than a 1-hour total collection and processing period from time of blood draw, samples were subsequently transported on ice and centrifuged at 2000×*g* for 10 minutes, and the plasma was aliquoted into cryogenic vials and stored at –20°C (–4°F) or colder locally. They were subsequently shipped on dry ice to a centralized laboratory for storage (–70°C [–94°F]) and analysis. Although the protocol included subsequent serial blood sample collections (3, 6, 12, 24, 48, and 72 hours) according to patient availability, we used only time 0 NGAL for this analysis.

All plasma NGAL measurements were independently performed by a single laboratory (Biosite Incorporated, San Diego, CA) blinded to the clinical data. The immunoassay for NGAL was performed on the Triage platform on a 9-assay fluorescent microfluidic protein chip, as previously described.¹⁰ The Triage platform is a point-of-care system designed for bedside use, whose on-board algorithm is capable of reporting a test result within 15 to 25 minutes. The plasma NGAL lower limit of detection was 50 ng/mL and the upper limit of the assay range was 2,000 ng/mL.

Outcome Measures

Acute kidney injury was defined as a serum creatinine level increase greater than 0.5 mg/dL or acute need for renal replacement therapy within 72 hours. The change in serum creatinine level was assessed between the enrollment blood draw and any of the blood draws at 12, 24, 48, and 72 hours postenrollment. The Risk, Injury, Failure, Loss of function, End-stage disease (RIFLE) criteria classify 3 types of groups: those with increased risk, those with renal injury, and those with renal failure.^{12–14} As secondary analysis, we used the RIFLE criteria for acute kidney injury and classified patients as having either no acute kidney injury or acute kidney injury, using 2 thresholds for severity: (1) RIFLE R and above, corresponding to a 1.5-fold increase in serum creatinine level; or (2) RIFLE I and above, corresponding to a 2-fold increase in serum creatinine level.^{12–14} Patients requiring acute dialysis were also classified as having acute kidney injury.

Primary Data Analysis

To assess for differences in median biomarker levels between patients with acute kidney injury, without acute kidney injury, and those who died, box plots are shown for plasma NGAL concentrations and serum creatinine concentrations at

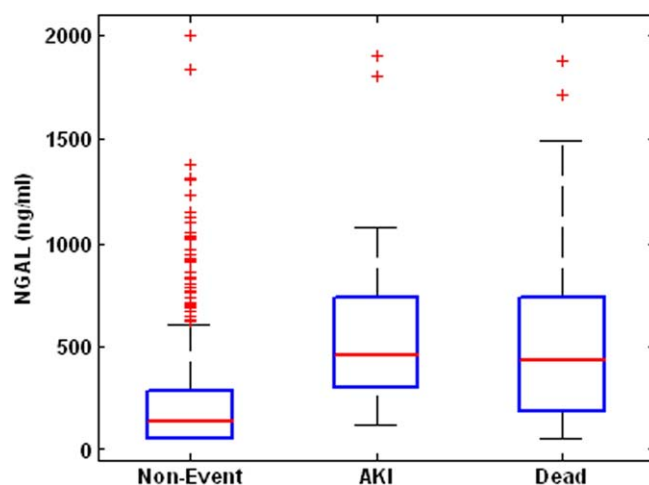


Figure 1. NGAL concentration and acute kidney injury. AKI, Acute kidney injury.

enrollment (Figure 1). To report the diagnostic accuracy, we report the operating characteristics of the markers, receiver operator characteristic curves were constructed for plasma NGAL and serum creatinine levels, and the area under the curve as a predictor of acute kidney injury is calculated for each. Cutoffs were determined by manual inspection of the receiver operator characteristic curves for the outcome of acute kidney injury; the sensitivity, specificity, and odds ratio were evaluated at each cutoff. The 95% confidence intervals (CIs) were estimated for the area under the curve according to the method of Hanley and McNeil.^{15,16} The 95% CIs for the odds ratio assume a normal distribution and for sensitivity and specificity, assume binomial distributions. Finally, to perform a sensitivity analysis of the results limiting the patients to those with likely new kidney injury, we exclude patients presenting with a creatinine level greater than 2.0 mg/dL and report the operating characteristics of this population. Data analysis was performed in MatLab 7.5.0.

RESULTS

Characteristics of Study Subjects

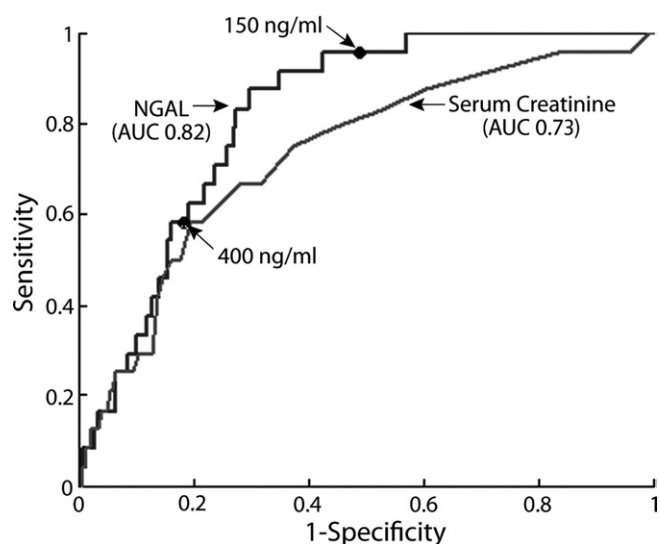
A total of 1,015 ED patients were enrolled across the 10 centers in the United States in the original population, as described previously. For the analysis of acute kidney injury, the population was further restricted to exclude all patients with a history of chronic dialysis (*n* = 78), patients who did not have an ED presentation value for NGAL (*n* = 30), patients who did not have an ED presentation value for serum creatinine (*n* = 19), and patients who did not have at least 1 subsequent serum creatinine laboratory result in 12 to 72 hours after presentation (*n* = 227, of whom 4 died before 72 hours). This resulted in a subset of 661 patients for whom analysis was performed. Table 1 shows the demographics and the relevant baseline physiologic and laboratory variables for these 661 patients, as well as for the 354 patients excluded because of the reasons outlined above.

Table 1. Demographics and baseline physiologic and laboratory variables.

Characteristics	Included Subjects (n=661)	Excluded Subjects (n=354)
Age, y, mean (SD)	59 (19)	48 (18)
Sex, % female	52	55
Race, No. (%)		
White	346 (52)	149 (42)
Black	242 (37)	168 (47)
Hispanic	51 (8)	29 (8)
Asian	11 (2)	3 (1)
Native American	1 (0)	0
Other	10 (2)	5 (1)
Comorbidities, No. (%)		
Hypertension	314 (48)	147 (42)
Cardiovascular disease	180 (27)	59 (17)
Diabetes	188 (28)	93 (26)
Immunocompromised	119 (18)	43 (12)
End-stage renal disease/hemodialysis	0	78 (22)
Stroke	78 (12)	18 (5)
Cirrhosis	20 (3)	9 (3)
Temperature, °C, mean (SD)	38.1 (1.3)	38.3 (1.1)
Pulse rate, beats/min, mean (SD)	110 (20)	108 (17)
Respiratory rate, breaths/min, mean (SD)	22 (6)	21 (5)
Systolic blood pressure, mm Hg, mean (SD)	122 (29)	126 (28)
WBC count, 1,000/mm ³ , mean (SD)	14.4 (8.9)	12.2 (6.7)
Platelet count/mm ³ , mean (SD)	278 (282)	251 (153)
Blood urea nitrogen, mg/dL, mean (SD)	27 (25)	21 (20)
Creatinine, serum, mg/dL, mean (SD)	1.4 (1.1)	2.4 (2.7)

There were 24 (1.7%) patients who satisfied the criteria of acute kidney injury defined by a greater than 0.5 mg/dL increase in serum creatinine level at 12, 24, 48, or 72 hours relative to the level at enrollment or required renal replacement therapy or dialysis. Of the 24 patients who had acute kidney injury, 6 went on to require dialysis; 3 of these patients had a greater than 0.5 mg/dL increase in serum creatinine level before the initiation of dialysis, 2 of these patients had highly increased serum creatinine levels (>5 mg/dL) at enrollment and required dialysis within 72 hours, and 1 patient had an increased serum creatinine level at enrollment (2.6 mg/dL) that decreased during the following 72 hours without dialysis, but subsequently developed the need for dialysis at day 17 of the hospital stay.

Figure 1 shows a box plot of plasma NGAL levels assayed from plasma samples obtained at ED presentation. The patient groups for this analysis are (a) nonevent (n=585), (b) acute kidney injury within 72 hours of enrollment (n=24, of whom 7 died inhospital), and (c) inhospital mortality excluding acute kidney injury (n=52, of whom 12 died before 72 hours). The median NGAL levels were nonevent 134 ng/mL (interquartile range [IQR] 57 to 277 ng/mL), acute kidney injury 456 ng/mL (interquartile range 296 to 727 ng/mL), and death excluding acute kidney injury 431 ng/mL (interquartile range 188 to 736 ng/mL). Thus, plasma NGAL levels in the group with acute kidney injury are 3.4-fold higher than plasma NGAL levels in the nonevent group. NGAL concentrations were also very high

**Figure 2.** Acute kidney injury within 72 hours of enrollment.

in the 12 patients who died before 72 hours (median 876 ng/mL; IQR 292 to 1,184 ng/mL). For initial creatinine, the median levels were nonevent 1.1 mg/dL (IQR 0.8 to 1.5 mg/dL), acute kidney injury 1.9 mg/dL (interquartile range 1.3 to 3.0 mg/dL), and death excluding acute kidney injury 1.5 mg/dL (interquartile range 1.0 to 2.4 mg/dL). In patients with increased initial creatinine level above 2.0 mg/dL, the plasma NGAL levels in the nonevent group were increased (n=74; median 422 ng/mL; IQR 244 to 701 ng/mL) into the range of the acute kidney injury group (n=11; median 541 ng/mL; IQR 338 to 933 ng/mL).

To provide a perspective on NGAL's potential as a biomarker for acute kidney injury, we show receiver operator characteristic curves for both NGAL and initial serum creatinine levels for the group of patients developing acute kidney injury versus all other possible outcomes (Figure 2). Plasma NGAL level was found to be a strong predictor of acute kidney injury, with an area under the curve of 0.82 (95% CI 0.76 to 0.88). Serum creatinine level was also a strong predictor of acute kidney injury, with area under the curve of 0.73 (95% CI 0.63 to 0.84). The plasma NGAL level corresponding to the 95th percentile of normal healthy donors is reported to be approximately 150 ng/mL. In this ED population for the outcome of acute kidney injury, plasma NGAL levels greater than 150 ng/mL were 96% sensitive (95% CI 79% to 100%) and 51% specific (95% CI 47% to 55%), with an odds ratio of 24 (95% CI 3.3 to 181). In comparison, to achieve the same sensitivity with serum creatinine level at ED presentation a cutoff of 0.7 mg/dL was required, which corresponds to a specificity of 17% (95% CI 14% to 20%). At higher cutoff levels corresponding to lower sensitivity but higher specificity, eg, NGAL level greater than 400 ng/mL and creatinine level greater than 1.7 mg/dL, the 2 assays exhibit similar performance. These results are summarized in Table 2, and Appendix E1 (available online at <http://www.annemergmed.com>).

Table 2. Operating characteristics of NGAL and creatinine.

	Odds Ratio	(95% CI)	Sensitivity	(95% CI)	Specificity	(95% CI)
AKI within 72 h, 24 cases of 661 patients						
NGAL <150	24.3	(3.3–181)	0.96	(0.79–1.00)	0.51	(0.47–0.55)
sCr >0.7	4.64	(0.62–35)	0.96	(0.79–1.00)	0.17	(0.14–0.20)
NGAL >400	6.35	(2.8–14)	0.58	(0.37–0.78)	0.82	(0.79–0.85)
sCr >1.7	5.79	(2.5–13)	0.58	(0.37–0.78)	0.81	(0.77–0.84)
AKI within 72 h, using RIFLE R as severity threshold, 27 cases of 661 patients						
NGAL >150	4.6	(1.7–12)	0.81	(0.62–0.94)	0.51	(0.47–0.55)
sCr >0.7	0.85	(0.3–2.3)	0.81	(0.62–0.94)	0.16	(0.13–0.19)
NGAL >400	4.9	(2.2–11)	0.52	(0.32–0.71)	0.82	(0.79–0.85)
sCr >1.7	3.2	(1.5–7.0)	0.44	(0.25–0.65)	0.80	(0.77–0.83)
AKI within 72 h, using RIFLE I as severity threshold, 15 cases of 661 patients						
NGAL >150	14.4	(1.9–110)	0.93	(0.68–1.00)	0.51	(0.47–0.55)
sCr >0.7	2.8	(0.36–21)	0.93	(0.68–1.00)	0.17	(0.14–0.20)
NGAL >400	12.3	(3.8–39)	0.73	(0.45–0.92)	0.82	(0.79–0.85)
sCr >1.7	4.5	(1.6–13)	0.53	(0.27–0.79)	0.80	(0.77–0.83)
Inhospital mortality, 59 cases of 661 patients						
NGAL >150	5.49	(2.7–11)	0.83	(0.71–0.92)	0.53	(0.49–0.57)
sCr >0.7	1.27	(0.58–2.8)	0.86	(0.75–0.94)	0.17	(0.14–0.20)
NGAL >400	6.17	(3.5–11)	0.54	(0.41–0.67)	0.84	(0.81–0.87)
sCr >1.7	2.94	(1.7–5.1)	0.41	(0.28–0.54)	0.81	(0.78–0.84)

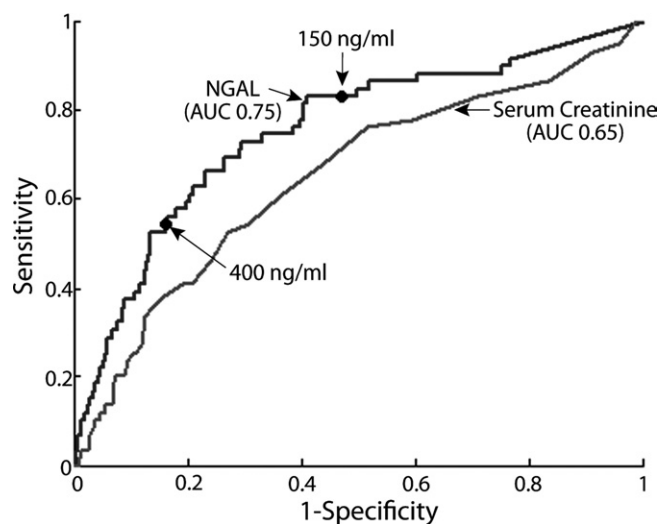
sCr, Serum creatinine.

Clinical performance metrics comparing plasma NGAL and sCr for prediction of AKI within 72 hours of enrollment, RIFLE-R within 72 hours, RIFLE-I within 72 hours, and all-cause in-hospital mortality within 72 hours. Cutoffs for NGAL were taken by visual inspection of the receiver operator characteristic curve for AKI within 72 hours. The corresponding cutoffs for sCr were selected to match plasma NGAL sensitivity for AKI within 72 hours. The odds ratio was evaluated at each cutoff according to a 2×2 contingency table comparing all patients above the cutoffs with all patients at or below the cutoff. The same cutoff concentrations were applied to AKI within 72 hours, as defined by RIFLE R threshold; AKI within 72 hours, as defined by the RIFLE I threshold; and all-cause in-hospital mortality. Concentrations are in units of nanograms per milliliter for NGAL and milligrams per deciliter for sCr.

There are many criteria in the literature for describing or classifying the severity of acute kidney injury, of which RIFLE criteria have been well accepted.^{13,14,17} Following the creatinine criteria of RIFLE, the 661 patients in this study were classified as having either no acute kidney injury or acute kidney injury, using 2 thresholds for severity: RIFLE R and above and RIFLE I and above (see “Materials and Methods” section for details), which we used as a secondary outcome. The results of this comparison are summarized in Table 2. The observations made about the utility of plasma NGAL and initial serum creatinine levels for the diagnosis of acute kidney injury are consistent, whether the outcomes are defined by our previously described criteria for acute kidney injury or defined by the RIFLE criteria at either of the 2 severity thresholds of R or I.

The receiver operator characteristic curves for plasma NGAL and serum creatinine levels for the prediction of all-cause in-hospital mortality (59 patients of 661) are shown in Figure 3. The area under the curve for NGAL is 0.75 (95% CI 0.68 to 0.82), and the area under the curve for serum creatinine is 0.65 (95% CI 0.57 to 0.73). The results comparing plasma NGAL and serum creatinine performance for predicting in-hospital mortality, using various cutoffs, are also included in Table 2.

Patients with high serum creatinine level on ED presentation are known to be at greater risk for acute kidney injury. NGAL may be particularly useful in patients presenting with lower serum creatinine level, who would otherwise not be identified. After excluding patients with initial serum creatinine level

**Figure 3.** In-hospital death.

greater than 2.0 mg/dL, there remained a subgroup of 558 patients in this study, 13 of whom met the definition for acute kidney injury. In this subgroup, the area under the curve for acute kidney injury for NGAL was 0.84 (95% CI 0.77 to 0.92) compared with 0.67 (95% CI 0.51 to 0.83) for serum creatinine. The sensitivity for NGAL levels greater than 150 ng/mL for acute kidney injury was 92% (95% CI 64% to

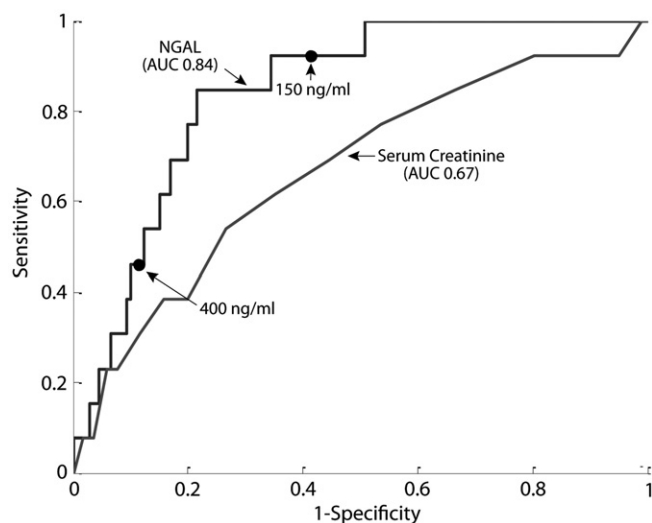


Figure 4. AKI within 72 hours of enrollment, excluding initial CR > 2.0.

100%), the specificity was 59% (95% CI 54% to 63%), and the odds ratio was 16.9 (95% CI 2.2 to 131). (Figure 4).

LIMITATIONS

There are a number of limitations to this study. First, because it was originally designed as a sepsis study, we did not include a broad ED population; instead, we limited it to patients with suspected sepsis. Because NGAL can be increased as part of the pathophysiology of sepsis, it is possible that this confounded our results. Second, in the original study cohort, there were a number of patients who did not have a follow-up serum creatinine measurement available and were not included in the current study, leaving our results open to selection bias. Next, the incidence and total number of patients meeting the outcome of acute kidney injury were low, making our point estimates imprecise. Iatrogenic kidney injury may have occurred after the NGAL measurement because agents such as antibiotics or intravenous contrast dye may have contributed to the development of acute kidney injury NGAL; however, we did not record the administration of these agents and cannot account for them in analysis, representing a limitation of the study. We used serum creatinine levels both as a comparator to assess NGAL performance and to define acute kidney injury, which is an incorporation bias. However, this would bias our results toward favoring serum creatinine, which they did not. It is clear that a larger study of a broad population with tighter follow-up and more cases of acute kidney injury is needed to more definitively define thresholds for abnormal results, as well as to validate these findings altogether. Finally, our study design did not allow us to assess whether the test would add to or improve clinical decisionmaking; this would need to be answered in a separate study once the cutoffs are prospectively derived and validated.

DISCUSSION

In patients presenting to the ED with suspected sepsis, NGAL appears to hold promise as a sensitive marker for acute kidney injury. At concentrations greater than 150 ng/mL, plasma NGAL was 95% sensitive for acute kidney injury. Using the serum creatinine values to assess the severity of acute kidney injury within 72 hours of presentation, plasma NGAL at a cutoff of 150 ng/mL was 93% sensitive at the RIFLE I threshold and 81% sensitive at the RIFLE R threshold. NGAL at this cutoff was also 83% sensitive for all-cause in-hospital mortality. The analogous high-sensitivity cutoff for acute kidney injury, using serum creatinine levels on presentation to the ED, would be 0.7 mg/dL, which provides inferior clinical utility. Therefore, plasma NGAL is a new and promising biomarker for early diagnosis of acute kidney injury.

There are several previous studies of NGAL both in urine and plasma that support its use as a biomarker of acute kidney injury. The utility of NGAL as a biomarker for early identification of acute kidney injury (defined as a 50% or greater increase in serum creatinine level) in humans was first described by Mishra et al⁴ in a study of 71 pediatric cardiopulmonary bypass surgery patients. In this study, plasma and urine NGAL levels at 2 hours after surgery had an area under the curve of 0.91 and 0.998, respectively, demonstrating excellent discrimination of acute kidney injury. Dent et al⁶ reported an area under the curve of 0.96 for the early identification of acute kidney injury in a cohort of 120 pediatric cardiopulmonary bypass surgery patients, using a recently developed standardized point-of-care plasma NGAL assay (Triage NGAL Test; Biosite Diagnostics). In a study of 143 critically ill children, Wheeler et al¹⁸ found increased median NGAL levels in comparing critically ill pediatric septic shock patients (median 302; IQR 151 to 570) with patients with systemic inflammatory response criteria (median 108; IQR 89 to 179), as well as controls (median 80; IQR 56 to 86), and, in patients with acute kidney injury (median 355; IQR 166 to 1,322) with those without (median 186; IQR 98 to 365). Further, in a study of percutaneous coronary intervention, plasma NGAL levels were found to increase significantly at 2 and 4 hours post-percutaneous coronary intervention in patients who developed contrast-induced nephropathy.¹⁹ More recent data have been published on the utility of NGAL in identifying patients admitted to the hospital from the ED who subsequently develop acute kidney injury. In this study, the sensitivity and specificity of a urine NGAL level measured by immunoblot for detecting acute kidney injury were 0.90 (95% CI 0.73 to 0.98) and 0.995 (95% CI 0.990 to 1.00), respectively.²⁰ Our study provides additional evidence of the utility of NGAL for acute kidney injury in a multicenter population. We used a rapid point-of-care platform to perform our assays, making NGAL testing in the ED feasible. This technology may facilitate earlier diagnosis of acute kidney injury if used at the bedside during the initial hospital contact.

Although our study shows an initial association between serum NGAL levels and the development of acute kidney injury, future studies designed specifically to address this question are warranted. We report the operating characteristics for 2 cutoffs for NGAL; however, these are meant to be illustrative, and larger studies are required to establish the final cutoffs that should be used in clinical practice. Additionally, because this was a secondary analysis, we unfortunately did not collect important data about whether patients were exposed to nephrotoxic agents such as intravenous contrast agents, antibiotics, or vasopressors that may have caused iatrogenic kidney injury after serum NGAL levels were sampled. This omission may have led to an increase in the false-negative rate for NGAL. Future studies should be mindful to address this concern. Finally, future studies should not only validate our findings but also test whether this (or any other biomarker) improves clinical decisionmaking at the bedside.

In conclusion, our findings support NGAL as a promising new biomarker for acute kidney injury in the acute setting. Our preliminary findings show an association, but a prospective study specifically designed to address this association is warranted. As we consider the potential for future clinical application, plasma NGAL measurements were generated with a point-of-care device that can provide quantitative results from whole blood or plasma in approximately 15 minutes. The device and this approach offer a practical opportunity, in a clinically useful manner, to improve bedside diagnosis of ED patients at risk for acute kidney injury.

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Address for correspondence: Nathan I. Shapiro, MD, MPH, Beth Israel Deaconess Medical Center, 1 Deaconess Rd, CC2-W, Boston, MA 02116; 617-754-2323, fax 617-754-2350; E-mail Nshapiro@bidmc.harvard.edu.

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IMAGES IN EMERGENCY MEDICINE

(continued from p. 18)

DIAGNOSIS:

Thrombotic occlusion of the superior mesenteric artery. The ultrasonography demonstrated a thrombus in the abdominal aorta that extended into the superior mesenteric artery (Figures 1 and 2). Emergency surgical consultation was obtained because of these findings. CT scan with intravenous contrast confirmed the presence of a filling defect consistent with the diagnosis of a proximal abdominal aortic and superior mesenteric artery thrombosis (Figure 3). In addition, the CT scan revealed a pulmonary embolus, left renal infarction, and small-bowel ischemia. Given the patient's advanced age and comorbidities, her family elected to provide comfort measures only. She did not receive anticoagulation but received intravenous antibiotics and fluids. She remained relatively stable despite a persistent tachycardia. After a short hospital stay, she was transferred back to her skilled nursing facility. Aortic thrombosis has been described in patients with neoplastic disease, aortic aneurysm, aortic dissection, and atherosclerosis. It is rare in the absence of these disease states.¹ Contributing factors in this case may include a presumed diagnosis of age-related atherosclerosis, early sepsis, and vascular stasis caused by dehydration.

Bedside emergency ultrasonography of the aorta has well-established clinical utility in identification of the normal aorta and abdominal aortic aneurysm.² Although ultrasonography alone is usually not sensitive enough to rule out aortic dissection or thrombus, routine scanning to rule out abdominal aortic aneurysm may occasionally identify these diagnoses.

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Appendix E1.

2×2 Tables and operating characteristics for selected NGAL thresholds.

1. NGAL >150.

	AKI	No AKI
NGAL >150	23	310
NGAL ≤150	1	327
Total	24	637

Sensitivity 96% (95% CI 79% to 100%), specificity 51% (95% CI 47% to 55%), positive likelihood ratio 2.0, and negative likelihood ratio 0.08.

2. NGAL >400.

	AKI	No AKI
NGAL >400	14	115
NGAL ≤400	10	522

Sensitivity 58% (95% CI 37% to 78%), specificity 82% (95% CI 79% to 85%), positive likelihood ratio 3.2, and negative likelihood ratio 0.5.

3. sCr >0.7.

	AKI	No AKI
sCr >0.7	23	530
sCr ≤0.7	1	107

Sensitivity 96% (95% CI 79% to 100%), specificity 17% (95% CI 14% to 20%), positive likelihood ratio 1.2, and negative likelihood ratio 0.3.

4. sCr >1.7.

	AKI	No AKI
sCr >1.7	14	124
sCr ≤1.7	10	513

Sensitivity 58% (95% CI 37% to 78%), specificity 82% (95% CI 79% to 85%), positive likelihood ratio 3.0, and negative likelihood ratio 0.5.